UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/599,877	06/23/2000	Johan Lennerstrand	TIBO-0011/VIP0007	1424

7590 10/12/2005

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
PARKIN, JEFFREY S	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 10/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/599,877	LENNERSTRAND ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 20-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

Detailed Office Action

37 C.F.R. § 1.114

A request for continued examination under 37 C.F.R. § 1.114, including the fee set forth in 37 C.F.R. § 1.17(e), was filed in this application after final rejection, on 19 September, 2005. Since this application is eligible for continued examination under 37 C.F.R. § 1.114, and the fee set forth in 37 C.F.R. § 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R. § 1.114. Applicants' submission filed on 19 September, 2005, has been entered.

Status of the Claims

Claims 1-9 and 20-23 are currently under examination.

35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a),

the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103© and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

The factual inquiries set forth in *Graham et al. v. John Deere Company of Kansas City et al.; Calmar, Inc. v. Cook Chemical Company; Colgate-Palmolive Company v. Same*, 148 U.S.P.Q. 459 (U.S. Sup. Ct. 1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103 are summarized as follows: 1) Determining the scope and contents of the prior art. 2) Ascertaining the differences between the prior art and the claims at issue. 3) Resolving the level of ordinary skill in the pertinent art. 4) Considering objective evidence present in the application indicating obviousness or unobviousness.

Claims 1-3, 5-9, and 20-23 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Meyer *et al.* (1999) in view of Ekstrand *et al.* (1996). The claims are directed toward an HIV RT assay to assess the resistance of any given RT sample to treatment with an HIV RT inhibitor. The claims require a reaction well with the following components: (i) at least one template for an HIV RT enzyme; (ii) at least one primer; (iii) at least one detectable dNTP substrate; (iv) at least one HIV RT inhibitor; and (v) at least one ribonucleotide chosen from ATP and GTP, or at least one pyrophosphate. Additional steps recite comparative steps involving both the wildtype and mutant RTs.

As previously set forth, Meyer *et al.* (1999) provide an HIV RT

enzymatic assay to examine mutant activity that employs at least one template, at least one primer, at least one RT inhibitor, and either ATP/GTP or pyrophosphate (see Experimental Procedures, p. 42). The authors reported (p. 35, rt. col.) that "we describe an in vitro assay that reproduces the essential in vivo properties of the AZT resistance mutants. HIV-1 RT containing the D67N, K70R, T215F, and K219Q amino acid substitutions (designated as 67/70/215/219 RT in this report) was much more efficient than WT RT at extending the primer past several potential termination sites in the presence of AZTTP when ATP was added to the reaction. Transfer of the AZTMP residue from the primer terminus to ATP to form dinucleoside polyphosphate and unblocked primer was enhanced in the 67/70/215/219 RT."

The authors also noted (see p. 35, last paragraph, rt. col.) that the "Addition of a ribonucleoside triphosphate (ATP) to the reaction mixture provided an acceptor for the nucleotide-dependent primer unblocking activity in which the AZTMP residue from the chain-terminated primer was transferred to ATP to form Ap_4AZT, and the primer was shortened by one residue and was no longer blocked to elongation". The authors finally conclude (see p. 36, rt. col.) that "by adding ATP at concentrations likely to be present in intact cells, we have established an in vitro system that reflects the in vivo properties of the 67/70/215/219 mutant virus." This teaching does not disclose an RT assay that employs a detectable dNTP.

However, as previously set forth, Ekstrand *et al.* (1996) provide a non-radioactive reverse transcriptase assay that employs 5-bromodeoxyuridine 5'-triphosphate (BrdUTP) as the detectable dNTP (see Materials and Methods, p. 97). The assay described employs an alkaline phosphatase-conjugated anti-BrdU antibody and provides quantitative results. The authors note (see p. 104, last

paragraph) "the present paper describes a simple, sensitive and non-radioactive RT assay with kinetic features similar to those observed when the natural dTTP substrate is used."

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to utilize the detection format described by Ekstrand *et al.* (1996), in the RT assay provided by Meyer *et al.* (1999), since this provides a rapid, quantitative, and non-radioactive means for detecting the products of reverse transcription.

Applicants argue that unexpected results were obtained using the claimed invention. However, it is not readily manifest what type of results were actually obtained since the response failed to point to any particular experimental data. Applicants again contend that sufficient motivation and a reasonable expectation of success were not present in the prior art. These arguments are clearly not persuasive in view of the prior art. Moreover, as previously set forth, the Examiner recognizes that references cannot be arbitrarily combined and that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references. *In re Nomiya*, 184 U.S.P.Q. 607 (C.C.P.A. 1975). However, there is no requirement that a motivation to make the modification be expressly articulated. The test for combining references is what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art. *In re McLaughlin*, 170 U.S.P.Q. 209 (C.C.P.A. 1971). References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. *In re Bozek*, 163 U.S.P.Q. 545 (C.C.P.A. 1969). As set forth *supra*, both the motivation and a reasonable expectation of success were present in the prior art. One of ordinary skill in the art would

have had sufficient motivation to utilize the detection format described by Ekstrand *et al.* (1996), in the RT assay provided by Meyer *et al.* (1999), since this would provide a rapid, quantitative, and non-radioactive means for detecting the products of reverse transcription.

Claim 4 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Meyer *et al.* (1999) in view of Ueno *et al.* (1995). The content of Meyer *et al.* (1999) is disclosed in the preceding paragraph. Meyer and colleagues do not describe the utilization of an art-recognized RT activity label such as a radioactive dNTP, although a labeled primer was employed. However, Ueno *et al.* (1995) describe standard HIV RT assays that employ art-recognized labels such as radioactive labeled dNTPs (see pp. 23605-23606, EXPERIMENTAL PROCEDURES, *Materials* and *Product Analysis*). Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to utilize a radiolabeled dNTP, as taught by Ueno *et al.* (1995), in the assay of Meyer *et al.* (1999), since this represents a standard and art-recognized means for detecting RT reaction products. Applicants' arguments are not convincing as noted in the preceding paragraph.

Prior Art of Relevance

The following prior art, which was not relied upon in the office action, is considered germane to applicant's disclosure:

- Shafer, R. W., et al., 1998, "Multiple concurrent reverse transcriptase and protease mutations and multidrug resistance of HIV-1 isolates from heavily treated patients.", Ann. Intern. Med. 128(11):906-11.

- Winters, M. A., et al., 1998, "A 6-Basepair Insert in the Reverse Transcriptase Gene of Human Immunodeficiency Virus Type 1 Confers Resistance to Multiple Nucleoside Inhibitors.", J. Clin. Invest. 102(10):1769-1775.

Both references disclose HIV-1 AZT resistant mutants carrying M41L/M184V/T215Y mutations.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571) 272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through

Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

03 October, 2005